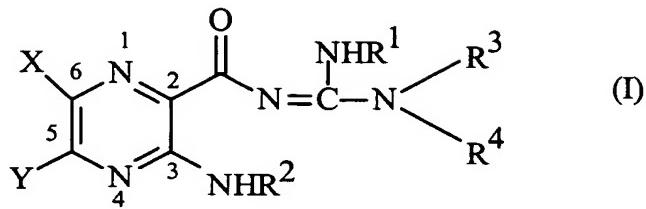


CLAIMS:

1. A compound represented by formula (I):



wherein

X is hydrogen, halogen, trifluoromethyl, lower alkyl, unsubstituted or substituted phenyl, lower alkyl-thio, phenyl-lower alkyl-thio, lower alkyl-sulfonyl, or phenyl-lower alkyl-sulfonyl;

Y is hydrogen, hydroxyl, mercapto, lower alkoxy, lower alkyl-thio, halogen, lower alkyl, unsubstituted or substituted mononuclear aryl, or -N(R<sup>2</sup>)<sub>2</sub>;

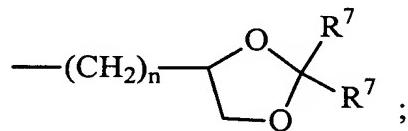
R<sup>1</sup> is hydrogen or lower alkyl;

each R<sup>2</sup> is, independently, -R<sup>7</sup>, -(CH<sub>2</sub>)<sub>m</sub>-OR<sup>8</sup>, -(CH<sub>2</sub>)<sub>m</sub>-NR<sup>7</sup>R<sup>10</sup>,

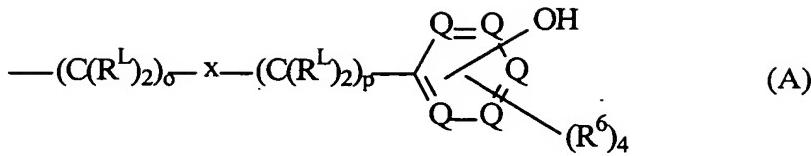
-(CH<sub>2</sub>)<sub>n</sub>(CHOR<sup>8</sup>)(CHOR<sup>8</sup>)<sub>n</sub>-CH<sub>2</sub>OR<sup>8</sup>, -(CH<sub>2</sub>CH<sub>2</sub>O)<sub>m</sub>-R<sup>8</sup>,

-(CH<sub>2</sub>CH<sub>2</sub>O)<sub>m</sub>-CH<sub>2</sub>CH<sub>2</sub>NR<sup>7</sup>R<sup>10</sup>, -(CH<sub>2</sub>)<sub>n</sub>-C(=O)NR<sup>7</sup>R<sup>10</sup>, -(CH<sub>2</sub>)<sub>n</sub>-Z<sub>g</sub>-R<sup>7</sup>, -(CH<sub>2</sub>)<sub>m</sub>-NR<sup>10</sup>-

CH<sub>2</sub>(CHOR<sup>8</sup>)(CHOR<sup>8</sup>)<sub>n</sub>-CH<sub>2</sub>OR<sup>8</sup>, -(CH<sub>2</sub>)<sub>n</sub>-CO<sub>2</sub>R<sup>7</sup>, or

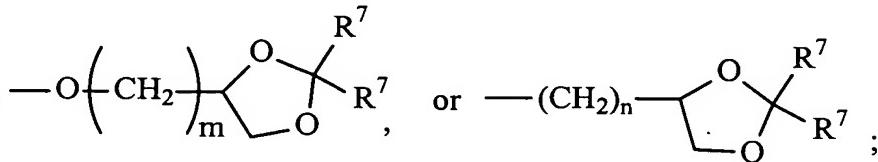


R<sup>3</sup> and R<sup>4</sup> are each, independently, hydrogen, a group represented by formula (A), lower alkyl, hydroxy lower alkyl, phenyl, phenyl-lower alkyl, (halophenyl)-lower alkyl, lower-(alkylphenylalkyl), lower alkoxyphenyl)-lower alkyl, naphthyl-lower alkyl, or pyridyl-lower alkyl, with the proviso that at least one of R<sup>3</sup> and R<sup>4</sup> is a group represented by formula (A):



wherein

- each  $R^L$  is, independently,  $-R^7$ ,  $-(CH_2)_n-OR^8$ ,  $-O-(CH_2)_m-OR^8$ ,
- $-(CH_2)_n-NR^7R^{10}$ ,  $-O-(CH_2)_m-NR^7R^{10}$ ,  $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,
- $-O-(CH_2)_m(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,  $-(CH_2CH_2O)_m-R^8$ ,
- $-O-(CH_2CH_2O)_m-R^8$ ,  $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$ ,
- $-O-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$ ,  $-(CH_2)_n-C(=O)NR^7R^{10}$ ,
- $-O-(CH_2)_m-C(=O)NR^7R^{10}$ ,  $-(CH_2)_n-(Z)_g-R^7$ ,  $-O-(CH_2)_m-(Z)_g-R^7$ ,
- $-(CH_2)_n-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,
- $-O-(CH_2)_m-NR^{10}-CH_2(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,
- $-(CH_2)_n-CO_2R^7$ ,  $-O-(CH_2)_m-CO_2R^7$ ,  $-OSO_3H$ ,  $-O$ -glucuronide,  $-O$ -glucose, or



each  $x$  is, independently,  $O$ ,  $NR^7$ ,  $C=O$ ,  $CHOH$ ,  $C=N-R^6$ , or represents a single bond;

each  $o$  is, independently, an integer from 0 to 10;

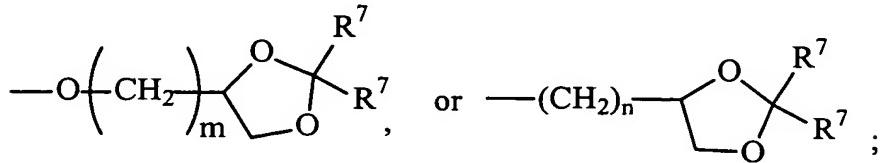
each  $p$  is, independently, an integer from 0 to 10;

with the proviso that (a) the sum of  $o$  and  $p$  in each contiguous chain is from 1 to 10 when  $x$  is  $O$ ,  $NR^7$ ,  $C=O$ , or  $C=N-R^6$  or (b) that the sum of  $o$  and  $p$  in each contiguous chain is from 4 to 10 when  $x$  represents a single bond;

each  $R^6$  is, independently,  $-R^7$ ,  $-OH$ ,  $-OR^{11}$ ,  $-N(R^7)_2$ ,  $-(CH_2)_m-OR^8$ ,

- $-O-(CH_2)_m-OR^8$ ,  $-(CH_2)_n-NR^7R^{10}$ ,  $-O-(CH_2)_m-NR^7R^{10}$ ,
- $-(CH_2)_n(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,  $-O-(CH_2)_m(CHOR^8)(CHOR^8)_n-CH_2OR^8$ ,
- $-(CH_2CH_2O)_m-R^8$ ,  $-O-(CH_2CH_2O)_m-R^8$ ,  $-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$ ,
- $-O-(CH_2CH_2O)_m-CH_2CH_2NR^7R^{10}$ ,  $-(CH_2)_n-C(=O)NR^7R^{10}$ ,

$-\text{O}-(\text{CH}_2)_m-\text{C}(=\text{O})\text{NR}^7\text{R}^{10}$ ,  $-(\text{CH}_2)_n-(\text{Z})_g-\text{R}^7$ ,  $-\text{O}-(\text{CH}_2)_m-(\text{Z})_g-\text{R}^7$ ,  
 $-(\text{CH}_2)_n-\text{NR}^{10}-\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$ ,  
 $-\text{O}-(\text{CH}_2)_m-\text{NR}^{10}-\text{CH}_2(\text{CHOR}^8)(\text{CHOR}^8)_n-\text{CH}_2\text{OR}^8$ ,  
 $-(\text{CH}_2)_n-\text{CO}_2\text{R}^7$ ,  $-\text{O}-(\text{CH}_2)_m-\text{CO}_2\text{R}^7$ ,  $-\text{OSO}_3\text{H}$ ,  $-\text{O}\text{-glucuronide}$ ,  $-\text{O}\text{-glucose}$ ,

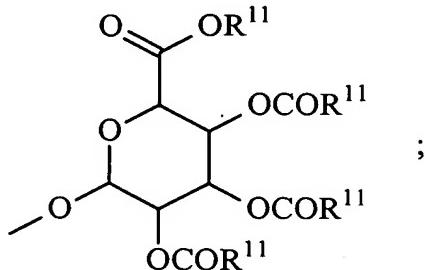


5 wherein when two  $\text{R}^6$  are  $-\text{OR}^{11}$  and are located adjacent to each other on a phenyl ring, the alkyl moieties of the two  $\text{R}^6$  may be bonded together to form a methylenedioxy group;

each  $\text{R}^7$  is, independently, hydrogen or lower alkyl;

each  $\text{R}^8$  is, independently, hydrogen, lower alkyl,  $-\text{C}(=\text{O})-\text{R}^{11}$ , glucuronide, 2-

10 tetrahydropyranyl, or



each  $\text{R}^9$  is, independently,  $-\text{CO}_2\text{R}^7$ ,  $-\text{CON}(\text{R}^7)_2$ ,  $-\text{SO}_2\text{CH}_3$ , or  $-\text{C}(=\text{O})\text{R}^7$ ;

each  $\text{R}^{10}$  is, independently,  $-\text{H}$ ,  $-\text{SO}_2\text{CH}_3$ ,  $-\text{CO}_2\text{R}^7$ ,  $-\text{C}(=\text{O})\text{NR}^7\text{R}^9$ ,

$-\text{C}(=\text{O})\text{R}^7$ , or  $-\text{CH}_2-(\text{CHOH})_n-\text{CH}_2\text{OH}$ ;

15 each  $\text{Z}$  is, independently,  $\text{CHOH}$ ,  $\text{C}(=\text{O})$ ,  $\text{CHNR}^7\text{R}^{10}$ ,  $\text{C}=\text{NR}^{10}$ , or  $\text{NR}^{10}$ ;

each  $\text{R}^{11}$  is, independently, lower alkyl;

each  $\text{g}$  is, independently, an integer from 1 to 6;

each  $\text{m}$  is, independently, an integer from 1 to 7;

each  $\text{n}$  is, independently, an integer from 0 to 7;

20 each  $\text{Q}$  is, independently,  $\text{C}-\text{R}^5$ ,  $\text{C}-\text{R}^6$ , or a nitrogen atom, wherein at most three  $\text{Q}$  in a ring are nitrogen atoms;

or a pharmaceutically acceptable salt thereof, and  
inclusive of all enantiomers, diastereomers, and racemic mixtures thereof.

2. The compound of Claim 1, wherein Y is -NH<sub>2</sub>.
- 5      3. The compound of Claim 2, wherein R<sup>2</sup> is hydrogen.
4. The compound of Claim 3, wherein R<sup>1</sup> is hydrogen.
5. The compound of Claim 4, wherein X is chlorine.
6. The compound of Claim 5, wherein R<sup>3</sup> is hydrogen.
7. The compound of Claim 6, wherein each R<sup>L</sup> is hydrogen.
- 10     8. The compound of Claim 7, wherein o is 4.
9. The compound of Claim 8, wherein p is 0.
10. The compound of Claim 9, wherein x represents a single bond.
11. The compound of Claim 10, wherein each R<sup>6</sup> is hydrogen.
12. The compound of Claim 11, wherein at most one Q is a nitrogen atom.
- 15     13. The compound of Claim 12, wherein no Q is a nitrogen atom.
14. The compound of Claim 1, wherein  
X is halogen;  
Y is -N(R<sup>7</sup>)<sub>2</sub>;
- 18     R<sup>1</sup> is hydrogen or C<sub>1</sub>-C<sub>3</sub> alkyl; and  
R<sup>2</sup> is -R<sup>7</sup>, -(CH<sub>2</sub>)<sub>m</sub>-OR<sup>7</sup>, or -(CH<sub>2</sub>)<sub>n</sub>-CO<sub>2</sub>R<sup>7</sup>;

R<sup>3</sup> is a group represented by formula (A); and

R<sup>4</sup> is hydrogen, a group represented by formula (A), or lower alkyl;

15. The compound of Claim 14, wherein

X is chloro or bromo;

5 Y is -N(R<sup>7</sup>)<sub>2</sub>;

R<sup>2</sup> is hydrogen or C<sub>1</sub>-C<sub>3</sub> alkyl;

at most three R<sup>6</sup> are other than hydrogen as defined above;

at most three R<sup>L</sup> are other than hydrogen as defined above; and

at most 2 Q are nitrogen atoms.

10 16. The compound of Claim 15, wherein Y is -NH<sub>2</sub>.

17. The compound of Claim 16, wherein

R<sup>4</sup> is hydrogen;

at most one R<sup>L</sup> is other than hydrogen as defined above;

at most two R<sup>6</sup> are other than hydrogen as defined above; and

15 at most 1 Q is a nitrogen atom.

18. The compound of Claim 17, wherein x is O, NR<sup>7</sup>, C=O, CHOH, or C=N-R<sup>6</sup>.

19. The compound of Claim 17, wherein x represents a single bond.

20 20. The compound of Claim 1, wherein x is O, NR<sup>7</sup>, C=O, CHOH, or C=N-R<sup>6</sup>.

21. The compound of Claim 1, wherein x represents a single bond.

20 22. The compound of Claim 1, wherein each R<sup>6</sup> is hydrogen.

23. The compound of Claim 1, wherein at most two R<sup>6</sup> are other than hydrogen as defined in Claim 1.

24. The compound of Claim 1, wherein one R<sup>6</sup> is other than hydrogen as defined in  
Claim 1.

25. The compound of Claim 1, wherein one R<sup>6</sup> is -OH.

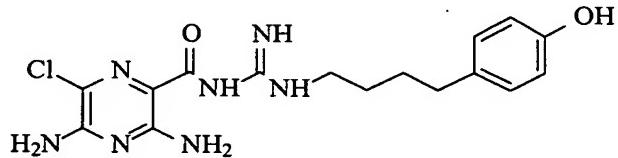
26. The compound of Claim 1, wherein each R<sup>L</sup> is hydrogen.

5 27. The compound of Claim 1, wherein at most two R<sup>L</sup> are other than hydrogen as  
defined in Claim 1.

28. The compound of Claim 1, wherein one R<sup>L</sup> is other than hydrogen as defined in  
Claim 1.

29. The compound of Claim 1, wherein x represents a single bond and the sum of o  
10 and p is 4 to 6.

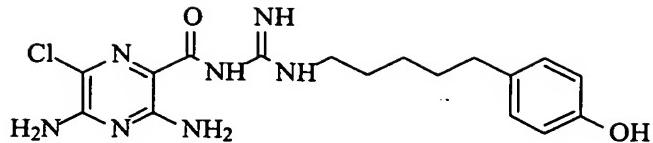
30. The compound of Claim 1, which is represented by the formula



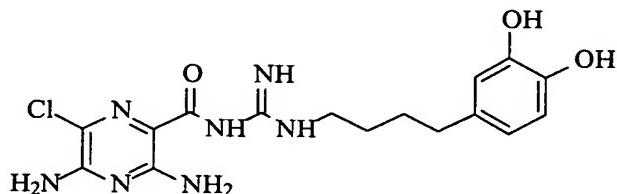
31. The compound of Claim 30, which is in the form of a pharmaceutically acceptable  
salt.

32. The compound of Claim 31, which is in the form of a hydrochloride salt.

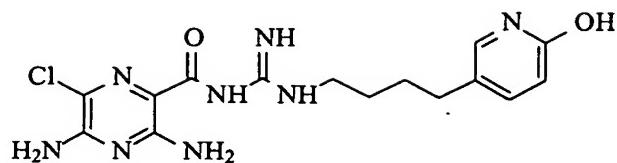
15 33. The compound of Claim 1, which is represented by the formula



34. The compound of Claim 33, which is in the form of a pharmaceutically acceptable salt.
35. The compound of Claim 34, which is in the form of a hydrochloride salt.
36. The compound of Claim 1, which is represented by the formula



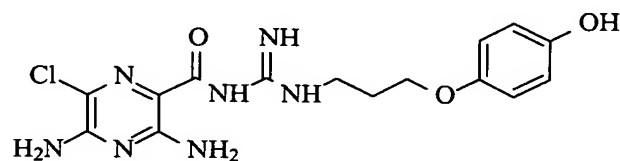
- 5       37. The compound of Claim 36, which is in the form of a pharmaceutically acceptable salt.
38. The compound of Claim 37, which is in the form of a hydrochloride salt.
39. The compound of Claim 1, which is represented by the formula



40. The compound of Claim 39, which is in the form of a pharmaceutically acceptable salt.

41. The compound of Claim 40, which is in the form of a hydrochloride salt.

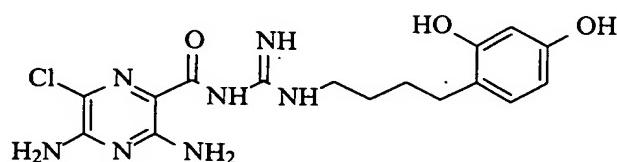
42. The compound of Claim 1, which is represented by the formula



5 43. The compound of Claim 42, which is in the form of a pharmaceutically acceptable salt.

44. The compound of Claim 43, which is in the form of a hydrochloride salt.

45. The compound of Claim 1, which is represented by the formula



46. The compound of Claim 45, which is in the form of a pharmaceutically acceptable salt.

47. The compound of Claim 46, which is in the form of a hydrochloride salt.

48. The compound of Claim 1, which is in the form of a pharmaceutically acceptable  
5 salt.

49. A pharmaceutical composition, comprising the compound of Claim 1 and a pharmaceutically acceptable carrier.

50. A method of promoting hydration of mucosal surfaces, comprising:  
administering an effective amount of the compound of Claim 1 to a mucosal surface of  
10 a subject.

51. A method of restoring mucosal defense, comprising:  
topically administering an effective amount of the compound of Claim 1 to a mucosal surface of a subject in need thereof.

52. A method of blocking sodium channels, comprising:  
15 contacting sodium channels with an effective amount of the compound of Claim 1.

53. A method of treating chronic bronchitis, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need  
thereof.

54. A method of treating cystic fibrosis, comprising:  
20 administering an effective amount of the compound of Claim 1 to a subject in need  
thereof.

55. A method of treating sinusitis, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

5 56. A method of treating vaginal dryness, comprising:  
administering an effective amount of the compound of Claim 1 to the vaginal tract of a subject in need thereof.

10 57. A method of treating dry eye, comprising:  
administering an effective amount of the compound of Claim 1 to the eye of a subject in need thereof.

58. A method of promoting ocular hydration, comprising:  
administering an effective amount of the compound of Claim 1 to the eye of a subject.

59. A method of promoting corneal hydration, comprising:  
administering an effective amount of the compound of Claim 1 to the eye of a subject.

60. A method of promoting mucus clearance in mucosal surfaces, comprising:  
15 administering an effective amount of the compound of Claim 1 to a mucosal surface of a subject.

61. A method of treating Sjogren's disease, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

20 62. A method of treating distal intestinal obstruction syndrome, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need thereof.

63. A method of treating dry skin, comprising:

administering an effective amount of the compound of Claim 1 to the skin of a subject in need thereof.

64. A method of treating esophagitis, comprising:

5 administering an effective amount of the compound of Claim 1 to a subject in need thereof.

65. A method of treating dry mouth (xerostomia), comprising:

administering an effective amount of the compound of Claim 1 to the mouth of a subject in need thereof.

10 66. A method of treating nasal dehydration, comprising:

administering an effective amount of the compound of Claim 1 to the nasal passages of a subject in need thereof.

67. The method of Claim 66, wherein the nasal dehydration is brought on by administering dry oxygen to the subject.

15 68. A method of preventing ventilator-induced pneumonia , comprising:

administering an effective amount of the compound of Claim 1 to a subject on a ventilator.

69. A method of treating asthma, comprising:

administering an effective amount of the compound of Claim 1 to a subject in need 20 thereof.

70. A method of treating primary ciliary dyskinesia, comprising:

administering an effective amount of the compound of Claim 1 to a subject in need thereof.

71. A method of treating otitis media, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need  
thereof.
- 5           72. A method of inducing sputum for diagnostic purposes, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need  
thereof.
- 10          73. A method of treating chronic obstructive pulmonary disease, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need  
thereof.
- 15          74. A method of treating emphysema, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need  
thereof.
- 20          75. A method of treating pneumonia, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need  
thereof.
- 25          76. A method of treating constipation, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need  
thereof.
- 30          77. The method of Claim 76, wherein the compound is administered orally or via a  
suppository or enema.
- 35          78. A method of treating chronic diverticulitis, comprising:  
administering an effective amount of the compound of Claim 1 to a subject in need  
thereof.

79. The present invention also provides a method of treating rhinosinusitis, comprising:

administering an effective amount of the compound of Claim 1 to a subject in need thereof.

5           80. A composition, comprising:  
the compound of Claim 1; and  
a P2Y2 inhibitor.

10          81. A composition, comprising:  
the compound of Claim 1; and  
a bronchodilator.